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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/021,753	10/30/2001	Ken Fujise	UTSH:251US	6306

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EXAMINER	
ANGELL, JON E	
ART UNIT	**PAPER NUMBER**
1635	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/11/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/021,753	FUJISE ET AL	
	Examiner	Art Unit	
	Jon Eric Angell	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 January 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-40 and 46-92* is/are pending in the application.

4a) Of the above claim(s) *1-38 and 49-62* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *39,40,46,47 and 63-92* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 October 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 1/5/07
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Action is in response to the communication filed on 1/19/2007.

The amendment filed 1/19/2007 is acknowledged and has been entered.

1. Applicant's arguments are addressed on a per section basis. The text of those sections of Title 35, U.S. Code not included in this Action can be found in a prior Office Action. Any rejections not reiterated in this action have been withdrawn as being obviated by the amendment of the claims and/or applicant's arguments.

Status of the Claims

Claims 1-40, 46-92 are currently pending in the application and are addressed herein.

Claims 1-38, 49-62 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 6/1/2004.

Claims 39, 40, 46, 47, 63-92 are examined herein.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 39, 40, 46, 47, 63-67, 84, 85, 90 and 92 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 39 is now drawn to: "A method for identifying a modulator of Fortilin polypeptide comprising: (a) contacting a Fortilin polypeptide with at least 90% of its amino acids identical with a candidate substance; and (b) assaying whether the candidate substance enhances or inhibits the Fortilin polypeptide activity, wherein a candidate substance that enhances or inhibits Fortilin polypeptide activity is a modulator of the Fortilin polypeptide. (Emphasis added)

As such, claim 39 encompasses a Fortilin polypeptide with at least 90% of its amino acids identical with a candidate substance. The claim does not explicitly identify what the Fortilin polypeptide is contacted with. Therefore claim 39, and all claims which depend thereon, are indefinite because it is unclear what the Fortilin polypeptide is contacted with. Additionally, it is unclear what "candidate substance" part (b) of the claim is referring to as part (a) is drawn a Fortilin polypeptide with at least 90% of its amino acids identical with a candidate substance, and does not explicitly indicate what the candidate substance is, or what the Fortilin polypeptide is contacted with.

Claim 92 is indefinite because it is not a complete sentence. Therefore the metes and bounds of the claim cannot be determined.

Additionally, claims 46, 47 and 92 depend on claim 41, which has been cancelled. Therefore, theses claims are indefinite for depending on a cancelled claim and the metes and bounds of the instant claims cannot be determined. Claims 46, 47 and 92 will not be considered further.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 39, 40, 63-67, 84, 85 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new matter rejection**.

37 CFR 1.118 (a) states that "No amendment shall introduce new matter into the disclosure of an application after the filing date of the application".

MPEP §2163.06 notes:

If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. In re Rasmussen, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981).

MPEP §2163.02 teaches that:

Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application.

MPEP §2163.06 further notes:

When an amendment is filed in reply to an objection or rejection based on 35 U.S.C. 112, first paragraph, a study of the entire application is often necessary to determine whether or not "new matter" is involved. Applicant should therefore specifically point out the support for any amendments made to the disclosure.

Claim 39 is now drawn to: "A method for identifying a modulator of Fortilin polypeptide comprising: (a) contacting a Fortilin polypeptide with at least 90% of its amino acids identical

with a candidate substance; and (b) assaying whether the candidate substance enhances or inhibits the Fortilin polypeptide activity, wherein a candidate substance that enhances or inhibits Fortilin polypeptide activity is a modulator of the Fortilin polypeptide. (Emphasis added).

The specification was thoroughly searched but support could be not found for "a Fortilin polypeptide with at least 90% of its amino acids identical with a candidate substance." Applicants have pointed to pages 9 and 27 for support for the new limitation; however, neither page 9 or 27 disclose a Fortilin polypeptide with at least 90% of its amino acids identical with a candidate substance. Therefore, the instant claims encompass limitations which were not present in the application as originally filed. As such, the instant claims are rejected for under 35 USC 112, first paragraph for having new matter. Should Applicants traverse, they are asked to indicate the specific page and line numbers of the specification where support can be found.

To the extent that the claimed compositions and/or methods are not described in the instant disclosure, the claims are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, since a disclosure cannot teach one to make or use something that has not been described.

Claims 68-83 and 86-89 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the

relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The Written Description Guidelines for examination of patent applications indicates, "the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, or by disclosure of relevant, identifying characteristics, i.e. structure or other physical and/or other chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show applicant was in possession of the claimed genus." (See MPEP 2100-164).

In the instant case, the claims encompass methods for identifying a modulator of "a Fortilin polypeptide" and encompass a Fortilin polypeptide that has "at least 90% of its amino acids identical or functionally equivalent to SEQ ID NO: 2" (see claim 68). As such, the claims encompass any polypeptide wherein at least 90% of its amino acids are functionally equivalent to the polypeptide of SEQ ID NO: 2. Therefore, the claims encompass a genus of polypeptides that is indeterminate in size, but which could potentially encompass an enormous number of different possible polypeptides, including polypeptides that have yet to be identified. It is noted that the claims specifically indicate that the polypeptides can be used to identify modulators of various Fortilin activities such as inhibition of apoptosis, binding to p53, binding to MCL1, cell cycle progression, etc. (e.g., see claims 71-74). Therefore, the claims clearly encompass variants that must have the same function as human Fortilin (SEQ ID NO: 2) because the variants must have human Fortilin activity in order for the variants to be useful in methods of identifying modulators of human Fortilin activity. For instance, the Fortilin polypeptides that are used in the

claimed methods to identify a modulator of p53-Fortilin interaction (e.g., claim 71) must possess the ability to interact with p53. The specification, however, has only disclosed one polypeptide that has all of the required functions to complete the claimed method: human Fortilin (SEQ ID NO: 2).

It is noted that the claims encompass a genus of polypeptides wherein 90% of the amino acids of the polypeptide are functionally equivalent to the amino acid sequence of SEQ ID NO: 2. This genus if polypeptides encompasses polypeptides that are completely different from SEQ ID NO: 2 (i.e., they are 0% identical to SEQ ID NO: 2). Accordingly, the claims encompass methods which utilize variant polypeptides of SEQ ID NO: 2 (human Fortilin) wherein the variant polypeptides could be any variant of Fortilin that meet the broad structural limitations of the claims, including non-functional variants and variants that have a different function. As such, the claims are drawn to the use of a polypeptide wherein the polypeptide can be any member of a huge genus of Fortilin polypeptides that meet the structural limitations of the claims. The specification has only described one species (SEQ ID NO: 2) of this vast genus that has the same functions as human Fortilin. The specification does not disclose any other variants of Fortilin that maintain the anti-apoptotic activity, or that bind to p53 or MCL1, or that are involved in cell cycle progression; nor does the specification indicate which amino acids of Fortilin can be changed or deleted and result in a biologically active Fortilin variant. Furthermore, there is no structure function relationship described such that one of skill in the art would be able to clearly recognize any structural elements critical for Fortilin functions disclosed in the specification. Considering the potentially vast number of variants encompassed by the claims and the limited guidance provided in the specification with respect to identifying the

biologically active variants encompassed by the claims, it is the Examiner's position that the specification has not adequately described a sufficient number of "representative species" encompassed by the claims, as required.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states, "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) In this case, the specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). For the reasons indicated herein, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of Fortilin polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, the claims encompass a genus of "Fortilin" polypeptides that includes variants of human Fortilin which are structurally and functionally different from those explicitly described in the specification. The claimed genus encompasses all possible "Fortilin"

polypeptide variants having at least 90% of its amino acids identical to or functionally equivalent to SEQ ID NO: 2 (a huge number of possibilities). However, the specification has not adequately described a sufficient number of species or the critical functional elements common to the members of the genus. Therefore, the written description requirement has not been met and the rejection is proper.

It is noted that the specification does provide description of one specific sequence which has anti-apoptotic activity: the human Fortilin polypeptide that is SEQ ID NO: 2. It is noted that limiting the claims to the Fortilin polypeptide that is SEQ ID NO: 2 would obviate this rejection.

Additionally, claims 39, 40 and 63-91 are also rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the claimed methods wherein (1) the Fortilin polypeptide that is contacted is isolated or in an isolated cell (e.g., see claim 39), (2) the recombinant cell that is contacted is an isolated cell (e.g., see claim 68), and (3) the Fortilin polypeptide has the amino acid sequence that is SEQ ID NO: 2; does not reasonably provide enablement for the full scope embraced by the claims. Specifically, the specification does not provide an enabling disclosure for performing the methods using a non-isolated cell, non-isolated Fortilin polypeptide (i.e., a cell or polypeptide that is in vivo), a non-isolated cell/polypeptide that is in a transgenic animal, or for the variant Fortilin polypeptides encompassed by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The claims are rejected essentially for the reasons of record, which are reiterated below, for convenience.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988).

> *Wands* states on page 1404,
> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention

The instant claims are drawn to a screening method for identifying a modulator of a Fortilin polypeptide. The specification discloses that Fortilin polypeptide can be in a cell (e.g., see claim 67); and further indicates that the method can be performed in an animal including a transgenic animal (e.g., see page 107, lines 13-14). Accordingly, the invention is in a class of invention which the CAFC has characterized as "the unpredictable arts such as chemistry and biology." Mycogen Plant Sci., Inc. v. Monsanto Co., 243 F.3d 1316, 1330 (Fed. Cir. 2001).

The breadth of the claims

The instant claims are very broad. For instance, claim 39 (and the claims which depend thereon) care drawn to "contacting a Fortilin polypeptide". Given the broadest reasonable interpretation, the phrase "contacting a Fortilin polypeptide" includes contacting a Fortilin polypeptide that is isolated as well as contacting a Fortilin polypeptide that is present in a cell. Claim 68 (and the claims which depend thereon) are drawn to contacting a candidate modulator with recombinant cell that expresses Fortilin. Given the broadest reasonable interpretation

consistent with the specification, these claims encompass contacting a non-isolated recombinant cell such as a recombinant cell that is part of a transgenic animal. It is noted that page 107, lines 13-14 indicate that the "[a]ssays may be conducted in cell free systems, in isolated cells, or in organisms including transgenic animals" (Emphasis added). Furthermore, Dr. Rick Wetsel states in the Declaration filed 2/21/06 that the cells of the transgenic animals could be considered recombinant cells (see page 5 of the Declaration). Therefore, it is reasonable to interpret all of the examined claims as encompassing method steps that are performed on non-isolated cells, including cells of a transgenic animal. It is noted that the claims are not limited to using any particular type of animal, as such; the claims encompass using any transgenic animal (i.e., a transgenic animal of any species).

Furthermore, claims encompass Fortilin polypeptides that have "at least 90% of [their] amino acids identical with a candidate substance" (claims 39, and "at least 90% of [their] amino acids identical with or functionally equivalent to SEQ ID NO: 2" (claim 68). Therefore, the claims encompass methods that utilize any species of a genus of Fortilin polypeptides wherein the Fortilin polypeptide can be a variant of SEQ ID NO:2 that has a function different from the function of SEQ ID NO:2. It is noted that the genus of Fortilin polypeptides encompassed by the claims is enormous considering that the genus encompasses any polypeptide that has 90% of its amino acids functionally equivalent to SEQ ID NO: 2.

The unpredictability of the art and the state of the prior art

As indicated above, the claims encompass methods that utilize transgenic animals. In order to use the transgenic animals in the claimed methods, it is necessary to be able to make the transgenic animals that expresses the Fortilin polypeptide. However, the prior art teaches that

making transgenic animals that express a functional transgene was unpredictable at the time the invention was made. For instance, the art of transgenic animals has for many years stated that the unpredictability lies with the site or sites of integration of the transgene into the target genome. Transgenic animals are regarded to have within their cells cellular mechanisms which prevent expression of the transgene, such as DNA methylation or deletion from the genome (**Kappel** et al (1992) Current Opinion in Biotechnology 3, 549, col. 2, parag. 2).

Furthermore, **Mullins et al.** states that not all animals express a transgene sufficiently expresses the transgene as the integration of a transgene into different species of animal has been reported to give divergent phenotypes (**Mullins et al.** (1993) Hypertension Vol. 22, page 631, col. 1, parag. 1, lines 14-17). Also, **Mullins et al**. (1996) teaches that "the use of nonmurine species for transgenesis will continue to reflect the suitability of a particular species for the specific questions being addressed, bearing in mind that a given construct may react very differently from one species to another." (**Mullins et al.** (1996) J. Clin. Invest. Vol. 97, page 1559, Summary).

Furthermore, well-regulated expression of the transgene is not frequently achieved because of poor levels or the complete absence of expression or leaky expression in non-target tissues (**Cameron** (1997) Molec. Biol. Vol. 7, page 256, col. 1 -2, bridg. parag.). Factors influencing low expression, or the lack thereof, are not affected by copy number and such effects are seen in lines of transgenic mice made with the same construct (**Cameron** (1997), page 256, lines 3-9). These factors, thus, are copy number independent and integration site dependent, emphasizing the role the integration site plays on expression of the transgene (**Cameron** (1997), page 256, lines 10-13).

While, the intent is not to say that genetically modified animals can never be made, the intent is to provide art taught reasoning as to why the instant claims are not enabled to their full scope. Given unpredictable nature with respect to properly expressing a transgene in an animal as well as the variability of transgene expression in different animal species, particularly when taken with the lack of specific guidance in the specification, it would have required undue experimentation to make the transgenic animals which have been engineered which are encompassed by the instant claims.

Additionally, the art recognizes that although structural similarity can serve to classify a protein as related to other known proteins, this classification is insufficient to establish a function or biological significance for the protein because ancient duplications and rearrangements of protein-coding segments have resulted in complex gene family relationships. Duplications can be tandem or dispersed and can involve entire coding regions or modules that correspond to folded protein domains. As a result, gene products may acquire new specificities, altered recognition properties, or modified functions. Extreme proliferation of some families within an organism, perhaps at the expense of other families, may correspond to functional innovations during evolution. See **Henikoff et al.** (Science 1997; previously cited). Accordingly, one skilled in the art would not accept mere homology as establishing a function of protein because gene products may acquire new specificities, altered recognition properties, or modified functions. Rather, homology complements experimental data accumulated for the homologous protein in understanding the homologous protein's biological role. Although, the presence of a protein module in a protein of interest adds potential insight into its function and guides experiments, insight into the biological function of a protein cannot be automated. However, homology can be

used to guide further research. (See Henikoff, paragraph bridging pages 613-614, through page 614, paragraph bridging columns 1-2).

Furthermore, the art recognizes that a high degree of structural homology may not result in functional homology. **Witkowski et al.** (Biochemistry 1999; previously cited) teaches that one amino acid substitution transforms a β-ketoacyl synthase into a malonyl decarboxylase and completely eliminates β-ketoacyl synthase activity. **Seffernick et al.** (J. Bacteriol., 2001; previously cited) teaches that two naturally occurring Pseudomonas enzymes having 98% amino acid sequence identity catalyze two different reactions: deamination and dehalogenation, therefore having different function. Therefore, the claimed genus of "Fortilin" polypeptides has the potential of encompassing polypeptides that have <u>different</u> functions.

Considering the teachings of Henikoff et al., Witkowski et al., and Seffernick et al., it is unpredictable that any of the Fortilin variants encompassed by the claims would have human Fortilin function which is required to identify modulators of Fortilin activity, as specifically claimed (e.g., see claims 46, 47, 71-74, etc.).

<u>Working Examples and Guidance in the Specification</u>

The specification does not provide any working examples which indicate that a transgenic animal of any kind (i.e., of any species) which properly expresses a sufficient amount of Fortilin polypeptide to be useful in the claimed methods has been made. Furthermore, the specification has only provided general guidance with respect to making the transgenic animals encompassed by the claims (e.g.,. see pages 105-106). However, these general references do not overcome the art-recognized problems which render the making of transgenic animals that properly express a sufficient level of a transgenic protein unpredictable.

Additionally, there are no techniques which have been disclosed in the specification or found in the relevant art which teach how to predictably perform the claimed assays on a non-isolated cell (e.g., an in vivo cell).

The specification discloses 7 specific sequence homologs of SEQ ID NO: 2 that meet the structural limitations of the claims (e.g., see Figure 1). The specification asserts that there are 3 domains of Fortilin, but does not disclose the specific function of each of the domains. The specification has disclosed a specific function for SEQ ID NO:2 as inhibiting p53-mediated apoptosis (e.g., Figure 5) and specifically binds to MCL-1 and p53 (e.g., see Examples 1 and 2). The specification does not disclose that any of the Fortilin homologs that are different from human Fortilin have the same function as human Fortilin and the categorization of the other polypeptides appears to be based solely on sequence homology.

Quantity of Experimentation

Considering the breadth of the claims, especially with respect to the number of different species of transgenic animals encompassed by the claims, and further considering that the prior art teaches that making transgenic animals is an unpredictable endeavor, the amount of additional experimentation required to be able to make the transgenic animals encompassed by the claims is enormous. For instance, additional experimentation would be required to show that a transgenic animal that properly expresses a sufficient amount of transgenic Fortilin polypeptide could be predictably made. Once this was completed, additional experimentation would be required to show that the different species of transgenic animals could be made that properly express a sufficient amounts of transgenic Fortilin polypeptide. Considering that the art teaches that different species of animals can express that same polypeptide differently (e.g., see Mullins 1996

as indicates above), the amount of additional experimentation required to show that the different species of transgenic animals encompassed by the claims could be predictably made is also enormous.

Furthermore, considering the breadth of the claims with respect to the number of different Fortilin polypeptides encompassed by the claims and considering that the specification has not adequately described the structural elements that are critical to function, additional experimentation would be required in order identify which variants of SEQ ID NO: 2 would be useful in the claimed methods and which ones would not be useful. That is, additional experimentation would be required in order to determine which variants encompassed by the claims could be used to identify a modulator of Fortilin activity and which ones would not be useful.

Level of the skill in the art

The level of the skill in the art is deemed to be high.

Conclusion

Considering the nature of the invention, the breadth of the claims, the unpredictable nature of the invention as recognized in the prior art, the lack of working examples and the limited guidance provided by the specification, as well as the high degree of skill required to practice the invention, it is concluded that the specification does not provide an enabling disclosure commensurate in scope with instant claims. Therefore, additional experimentation is required before one of skill in the art could predictably make and use the claimed invention to its full scope. The amount of additional experimentation required to perform the broadly claimed invention is undue.

Response to Arguments

Applicants' arguments filed 1/19/07 have been fully considered. Any rejections not reiterated in the instant Action have been withdrawn in view the amendment to the claims and/or applicants' arguments.

With respect to the rejection of claims under 35 USC 112, first paragraph (written description), Applicants argue that independent claims 39 and 68 are directed to methods involving a Fortilin polypeptide that has at least 90% of its amino acids identical to SEQ ID NO:2, which is 172 amino acids in length. Applicants assert that the genus of Fortilin polypeptides encompassed by the claims only includes polypeptides with fewer than 17 amino acid changes relative to SEQ ID NO:2. Applicants contend that in providing SEQ ID NO:2, the skilled artisan would readily appreciate that Applicants had described an adequate number of species that are covered by the claims and a computer program or a high school biology student could also discern the limited number of polypeptides covered by the claims.

In response, it is pointed out that claims 39 and 68 are not limited to methods involving a Fortilin polypeptide that has at least 90% of its amino acids identical to SEQ ID NO: 2. Rather, claim 39 is drawn to a method involving a Fortilin polypeptide with at least 90% of its amino acids identical with a candidate substance. Claim 39 does not identify the candidate substance as any particular substance, let alone SEQ ID NO: 2. Therefore, claim 39 is clearly not limited to polypeptides that are 90% identical to SEQ ID NO: 2. Furthermore, claim 68 is drawn to a method involving contacting a candidate modulator with a recombinant cell expressing a Fortilin polypeptide with at least 90% of its amino acids identical or functionally equivalent to SEQ ID

NO:2. Therefore, claim 68 is clearly not limited to polypeptides that are 90% identical to SEQ ID NO: 2. As indicated above, the claims encompass methods involving polypeptides which are not identical in structure to SEQ ID NO: 2 (human Fortilin), but which must have the same function as SEQ ID NO: 2. That is, in order for the claimed method to be able to identify a modulator of Fortilin polypeptide, the polypeptide used in the claimed methods must have the same function as Fortilin polypeptide. However, the specification does not provide a sufficient description of the structural elements of Fortilin polypeptide that are critical for its function to allow identification of the polypeptides encompassed by the claims which have Fortilin activity without performing additional experimentation.

Applicants contend that the reliance on *Fiddes v. Baird*, 30 USPQ2d 1481, and *Amgen Inc. v. Chugai Pharm. Co.*, 18 USPQ2d 1016 is inappropriate given that both of these cases involved claims with no structural limitations as set forth in the rejected claims because the instant claims are limited with respect to SEQ ID NO:2 and they disclose SEQ ID NO:2.

In response, the Examiner disagrees that *Fiddes v. Baird* and *Amgen Inc. v. Chugai Pharm. Co.* are inappropriate because both cases deal with claims which encompassed elements which were not adequately disclosed in the application. In the instant case, the claims encompass variants of SEQ ID NO: 2 which are not adequately described by the application. Therefore, *Fiddes v. Baird* and *Amgen Inc. v. Chugai Pharm. Co.* are appropriate.

It is noted that limiting the polypeptide to SEQ ID NO: 2 would obviate this rejection as the claims would not encompass the variant polypeptides which necessitate the rejection. Applicants' comments with respect to *Ex parte Friedberg* have been considered. Applicants are respectfully reminded that every case is decided on its own merits. (*See In re Giolito*, 530 F.2d

397, 400, 188 USPQ 645, 648 (CCPA 1976). That other applications have been determined to have sufficient description of for a claimed genus, based on different facts, is not evidence that the examiner's decision in this case, on these facts, is in error.

With respect to the rejection of claims under 35 USC 112, first paragraph (scope of enablement), Applicants take issue with the fact that the Action focuses on one particular embodiment--a recombinant cell that is in a transgenic animal--and argues that the claim is not enabled because of that one embodiment. Applicants contend that the claims are directed to a screening method which may or may not involve a recombinant cell, which may or may not be in a transgenic animal. There are many more embodiments of the claim that fully enabled and not contested by the Action. Applicants also contend that the evidence relied upon does not show that the prior art in the area of transgenic animals was unpredictable or that the invention could not be done.

In response, it is pointed out that limiting the claims to that which was indicated as being enabled would obviate the rejection. That is, limiting claim 39 to a method utilizing an isolated polypeptide and limiting claim 68 to a method utilizing an isolated cell which expresses the polypeptide would obviate the rejection as it applies to making and using the transgenic animals which are encompassed by the claims.

Applicant addresses each of the references cited in the rejection and appears to argue that each of the references does not teach that the invention could not be done.

In response, applicants' arguments have been fully considered, but are not persuasive. The references do not teach that it would be impossible to practice the claimed invention. The claims have been interpreted as encompassing performing the method steps in a transgenic animal (any type of animal) that has been genetically engineered to express the Fortilin polypeptide. The art teaches that making transgenic animals is an unpredictable endeavor.

Applicants also argue that the claims are directed to a Fortilin polypeptide that has at least 90% identity to the amino acid sequence of SEQ ID NO:2 and the scope of the claims is not very extensive because there can be at most 17 changes with respect to SEQ ID NO:2. Applicants assert that it would not require undue experimentation to evaluate different variations in the context of the claimed method.

In response, it is pointed out that the claims are not limited to methods involving a Fortilin polypeptide that has at least 90% of its amino acids identical to SEQ ID NO: 2 and which have at most 17 amino acids that are different from SEQ ID NO: 2. Claim 39 is drawn to a method involving a Fortilin polypeptide with at least 90% of its amino acids identical with a candidate substance. Claim 39 does not identify the candidate substance as any particular substance, let alone SEQ ID NO: 2. Therefore, claim 39 is clearly not limited to polypeptides that are 90% identical to SEQ ID NO: 2. Furthermore, claim 68 is drawn to a method involving contacting a candidate modulator with a recombinant cell expressing a Fortilin polypeptide with at least 90% of its amino acids identical or functionally equivalent to SEQ ID NO:2. Therefore, claim 68 is clearly not limited to polypeptides that are 90% identical to SEQ ID NO: 2. As such, the claims encompass using a vast number of different polypeptides sequences and an undue amount of additional experimentation required to determine which polypeptides encompassed by

the claims could be used in the method and which ones would not be functional and wouldn't be useful in the claimed methods.

It is noted that limiting the claims to methods that utilize SEQ ID NO: 2, rather than the variants that the claims now encompass, would obviate the rejection as it pertains to

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon Eric Angell whose telephone number is 571-272-0756. The examiner can normally be reached on 9:00 a.m.- 5:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Douglas Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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